

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Giesbert RICHARD et al.  
Serial No.: New  
Filing Date: March 1, 2002  
For: METHODS OF DIAGNOSING OR PROGNOSTICATING AGE-RELATED MACULAR DEGENERATION

PRELIMINARY AMENDMENT

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

IN THE SPECIFICATION

On page 1, immediately following the title, please insert the following sentence: --This is a nationalization of PCT/EP00/08554 filed September 1, 2000 and published in English.--

IN THE CLAIMS

Please amend claims 4, 7-9, 12-17, 22, 24, 28, 31-33 & 37 as follows:

4. (amended) The method according to claim 1, wherein said sample is taken from a body fluid, a tissue, or an organ, in particular an eye, of said subject.

7. (amended) The method according to claim 1, wherein a variation of said level of Cystatin C or a transcription product of a Cystatin C gene in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

8. (amended) The method according to claim 1, wherein a varied activity of Cystatin C in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

9.(amended) The method according to claim 1, wherein said Cystatin C gene is a polymorphic variant of the Cystatin C wild-type gene.

12. (amended) The method according to claim 1, wherein said subject is a human.

13.(amended) The method according to claim 1, wherein said Cystatin C is determined in its monomeric form.

14. (amended) The method according to claim 1, wherein at least one of said substances is detected using an immunoassay, an enzyme activity assay and/or a binding assay.

15. (amended) The method according to claim 1, wherein said reference value is that of a level, or an activity, or both said level and said activity, of at least one substance which is

selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein in a sample from a subject not suffering from said age- related macular degeneration.

16. (amended) The method according to claim 1, further comprising comparing a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, a transcription product of a gene coding for an amyloid protein in said sample with a level, an activity, or both said level level and said activity, of at least one of said substances in a series of samples taken from said subject over a period of time.

17. (amended) The method according to claim 1, wherein said subject receives a treatment prior to one or more of said sample gatherings.

22. (amended) The method of claim 19, further comprising: determining a level, or an activity, or both said level and said activity, of at least one substance which is selected from the group consisting of a transcription product of a Cystatin C gene, a translation product of a Cystatin C gene, a fragment of said translation product, an amyloid protein, and a transcription product of a gene coding for an amyloid protein, in a sample from said subject; and comparing said level, or said activity, or both

said level and said activity, of at least one of said substances to a reference value representing a known disease or health status.

24. (amended) The method according to claim 22, wherein a varied activity of Cystatin C in said sample from said subject relative to said reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of said age-related macular degeneration in said subject.

28. (amended) The use of a kit for diagnosis or prognosis of age-related macular degeneration, or for determination of increased risk of developing age-related macular degeneration, or for monitoring progression of age-related macular degeneration in said subject, or for monitoring success or failure of a therapeutic treatment of said subject, said kit comprising at least one reagent which is selected from the group consisting of (i) reagents that selectively detect a transcription product and/or a translation product of a Cystatin C gene, (ii) reagents that selectively detect a fragment of a translation product of a Cystatin C gene, (iii) reagents that selectively detect a mutation or polymorphism in a Cystatin C gene, and (iv) reagents that selectively detect a transcription product and/or a translation product of a gene coding for an amyloid protein for working the methods according to claim 1.

31. (amended) The method according to claim 29, wherein said agents are cathepsin derivatives or Cystatin C analogs.

32. (amended) The method according to claim 29, wherein per se known methods of gene therapy and/or antisense nucleic acid

technology are applied to administer said agent(s).

33. (amended) The method according to claim 29 comprising grafting donor cells into the eye of said subject, said subject or donor cells preferably treated so as to minimise or reduce graft rejection, - wherein said donor cells are genetically modified by insertion of at least one transgene encoding said agent(s).

37. (amended) The modulator of claim 34, wherein the modulator is capable of modulating a polymorphic variant of the wild-type Cystatin C gene, in particular a B allele.

**REMARKS**

The foregoing Preliminary Amendment is requested in order to delete the multiple dependent claims and avoid paying the multiple dependent claims fee.

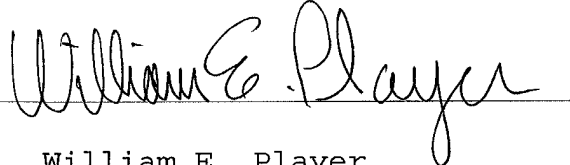
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Early action on the merits is respectfully requested.

Respectfully submitted,

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Atty. Docket: P67670US0  
Date: March 1, 2002  
WEP/cmf